REMARKS

Claim 31 has been amended to recite in the preamble "[a] system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase". In all instances the term "polysaccharide" has been replaced with "glycosaminoglycan". Support for the amendments is found in the Specification at, for example, page 28, line 27 – page 28, line 3; page 37, line 21 – 25; Examples 1 - 24 at page 38- 63 (see particularly page 38, lines 20 -26; page 40, line 26 – page 41, line 2; page 41, lines 8 - 9; page 41, line 28 – to page 42, line 2; page 42, line 7- 10; page 43, lines 1 – 5; page 45, lines 5 – 9; and page 48, line 17 – page 54, line 5 (Example 15)); and original claim 31. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Also, in the last line of claim 31, the word "an" has been replaced with "the" prior to "inhalable aerosol mist" in view of the recitation of "inhalable aerosol mist" added by amendment as noted above.

Claim 32 has been amended to replace "polysaccharide" with "glycosaminoglycan". Support for the amendment is found in the Specification at, for example, page 37, lines 21-25; and Examples 16 – 23 (pages 54 – 62).

Claim 33 has been amended to delete the word "said". The scope of the claim has not changed.

Claim 38 has been amended to replace "polysaccharide" with "glycosaminoglycan". Support for the amendment is found in the Specification at, for example, page 37, lines 21-25; and page 28, line 22 – page 34, line 17. The

amendment also recites the glycosaminoglycan "of the mixture" to provide antecedent support to amended claim 39.

Claim 39 has been amended to replace "solution" with "mixture". The amendment places the claim in conformity with formal requirements.

Claim 41 has been amended to replace "polysaccharide" with "glycosaminoglycan". Support for the amendment is found in the Specification at, for example, page 37, lines 21-25; page 27, line 24 – 29; and page 28, line 10 – page 37, line 19.

Claim 42 has been cancelled without prejudice.

Claim 43 has been amended to revise the dependency to that of claim 31.

Claim 44 has been amended to replace "polysaccharide" with "glycosaminoglycan". Support for the amendment is found in the Specification at, for example, page 37, lines 21-25; page 48, lines 17 – 20; and page 52, lines 21-25.

Claims 45, 46 and 47 have been amended to replace "polysaccharide" with "glycosaminoglycan". Support for the amendments is found in the Specification at, for example, page 37, lines 21-25; Examples 15 - 23 (page 48, line 17 – page 62, line 17); and page 21, lines 3-5.

Claim 48 has been added which obtains support from the Specification at, for example, Example 15, page 49, line 17 – page 54, line 5.

The amendments have been made without prejudice to submission of the non-amended claims in one or more continuing applications.

No new matter has been added by any of the amendments.

Obviousness Rejection

Claims 31-33 and 37-47 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cantor, U.S. Patent No. 5,633,003 ("Cantor") in combination with Green, WO 96/19968 ("Green"). (Paper 20081201 at 2.)

Cantor and Green have each been summarized previously on the record.

In making the rejection, the Examiner made the same assertions in the present Action, Paper No. 20081201 as in the prior Action, Paper 20080216, dated February 25, 2008. The Examiner's rejection was summarized in the Response to Office Action dated August 21, 2008.

It bears repeating that the Examiner acknowledged that "[t]he difference between applicants' claimed composition and the composition of Cantor is that Cantor does not disclose the concentration, molecular weight or particle size of the polysaccharide and [Cantor] does not use a drug or propellant." (Paper 20081201 at 4.)

In the "Response to Arguments" section addressing Applicants' prior arguments, the Examiner noted:

> The applicant argues that art subsequent to Cantor (the patent cited in the present rejection) reports that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. Cantor was filed in 1994 and issued in 1997. Horton and McKee published in 1999 and 1996, respectively. Following the publication of Horton in 1999, one skilled in the art would recognize at least these two reports evidencing a pro-inflammatory response associated with low molecular weight hyaluronic acid. (Paper No. 20081201 at 6.)

The Examiner asserted that "the rejection ... was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low

molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect [sic] aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teaching of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid is irrelevant. It should also be noted that the ... Horton and McKee references which were presented on the IDS dated 11/23/07 were previously considered by the examiner as indicated on the signed 1449 form mailed 02/25/08." (Id. at 6-7.)

The Examiner also noted that "[t]he applicant argues that in view of Horton and McKee, one skilled in the art would be led away from the presently claimed invention." (Id. at 7.) The Examiner repeated the same Horton/McKee mantra, that: "the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid

from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect [sic] aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates [sic] to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid is irrelevant." (Id.)

The Examiner also noted that "[t]he applicant argues that with respect to Horton and McKee, a *pro-inflammatory response in the airways* in connection with a *system for inhalable delivery* of the recited polysaccharide, the utility of which is *for treating or ameliorating the symptoms of a respiratory disorder,* is not fairly characterized as a 'side effect,' but rather, is in contradiction with the very purpose of the claimed system." (Id.)

The Examiner again relied on the same Horton/McKee mantra, that: "the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to

have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid or whether or not the said pro-inflammatory response is a side effect, is irrelevant." (Id. at 7-8.)

The Examiner further noted that "[t]he applicant argues that motivation to attain the claimed invention based on Cantor is lacking as Horton and McKee indicate that the claimed system for inhalable delivery of the recited polysaccharide for treating or ameliorating the symptoms of respiratory disease would become inoperable or have its intended function obliterated in view of a pro-inflammatory response as disclosed by Horton and McKee." (Id. at 8.)

The Examiner, using the same Horton/McKee mantra, asserted that: "the rejection ... was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see applicant's claim 31) and Cantor's disclose that that their composition comprising said polysaccharide treats respiratory disorders (i.e., it is operable). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different

molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect [sic] aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid or whether or not the said pro-inflammatory response is a side effect, is irrelevant." (Id. at 8-9.)

Arguments submitted on the record are incorporated here.

To forward prosecution in the present application, claim 31 has been amended to recite "[a] system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase." Also, the claim has further been amended to recite that the system comprises, *inter alia*, a mixture comprising a glycosaminoglycan having a molecular weight of between about 50,000 and 1.5×10^6 Daltons at a concentration of less than about 5.0 mg/ml (w/v) of glycosaminoglycan. In all instances, amended claim 31 recites a "glycosaminoglycan" in place of a "polysaccharide".

Cantor discloses a treatment of respiratory disorders by intratracheal administration. (Abstract.) Experimentals disclosed by Cantor "examined how lung hyaluronic acid content influences air-space enlargement in elastase-induced emphysema. (Col. 3, lines 21-23.) Cantor discloses that "hyaluronic acid has no elastase inhibitory capacity...". (Col. 3, lines 34-35.) Cantor further discloses that "further work will determine how hyaluronic acid influences air-space enlargement and

will evaluate the potential use of this substance as a treatment for emphysema." (Col. 3, lines 41-44.)

It is respectfully submitted that Cantor provides no motivation nor expectation of success for one skilled in the art to attempt to use a glycosaminoglycan in a system for pulmonary delivery to a mammal as an inhalable aerosol mist in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase. Nor would one skilled in the art have been led to the parameters of the claimed mixture comprising a glycosaminoglycan having a molecular weight of between about 50,000 and 1.5 x 10^6 Daltons at a concentration of less than about 5.0 mg/ml (w/v) of glycosaminoglycan.

As would have been known by one skilled in the art, formulation for aerosol delivery is complicated by many factors such as loss of the delivered agent during inhalation, dosing difficulties, enzymatic degredation in the lung, the complex anatomical structure of the respiratory system of a mammal including structures divided into many folds, non-uniform distribution of agents, varying effects of different molecular weight particles within the lungs as well as delivery of a desired molecular weight agent in relation to that administered, particle size distribution, etc. Delivery of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase is further complicated in that coating to protect the fibers involves achieving a sufficient coating of fibers on the lung surfaces, rather than aerosol delivery of an agent for absorption by lung tissue, where the agent is, for example, a drug or in some cases a polypeptide.

One skilled in the art would also have known that numerous formulation and delivery parameters would be available. Yet achieving a system for pulmonary delivery in which the recited parameters are shown to achieve the desired result would not have been predictable to one of skill in the art. Stated another way, known options for formulation and delivery of an agent in various combinations would not have provided predictable results in achieving a system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase.

In connection with the presently claimed invention, a system is recited which is "for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase." As disclosed in the Specification, the system as presently claimed provides a more uniform distribution of hyaluronic acid to elastic fibers than that seen with intratracheal instillation which resulted in a "patchy" distribution. (Specification, Page 41, Examples 5 and 6, pages 40 and 41.) In addition, the claimed system comprises, *inter alia*, "a mixture comprising a glycosaminoglycan having a molecular weight of between about 50,000 and 1.5 x 10^6 Daltons at a concentration of less than about 5.0 mg/ml (w/v) of glycosaminoglycan. The claimed system achieves delivery of a controlled molecular weight of glycosaminoglyacan, with only +/- 5% difference in molecular weight resulting from the aerosolization process. (Specification, example 24, pages 63-64.) Also, the recited molecular weight range has been identified in the face of a broad range of options and considerations, some which would have counseled one skilled in the art toward a higher range molecular weight. (See

Specification, for example, page 19, line 17 – page 21, line 27.) Example 15 (pages 48-54) discloses study results of protective effects found with various glycosaminoglycans.

It is submitted that one skilled in the art would not have predicted which formulation, if any, given numerous parameters for consideration, would provide a successful system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase, such that uniform distribution of hyaluronic acid to elastic fibers and a controlled delivery of desired molecular weight of glycosaminoglycan is achieved. Known options for combination, in this case for formulating for pulmonary delivery as recited, were not "finite, identified, and predictable", as in the facts presented in *KSR Int. Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007). In *Abbott Labs. v. Sandoz, Inc.*, 89 USPQ 1161, 1171 (Fed. Cir. 2008), the Court of Appeals for the Federal Circuit indicated that the Supreme Court in *KSR* "did not create a presumption that all experimentation in fields where there is already a background of useful knowledge is "obvious to try," without considering the nature of the science or technology." Indeed, the Federal Circuit has recently reiterated that "merely [throwing] metaphorical darts at a board filled with combinatorial prior art possibilities" is the epitome of impermissible hindsight reconstruction. *In re Kubin*, slip op. 2008-1184, 14 (Fed. Cir. April 3, 2009).

As in the *Abbott* case involving the problem of producing extended release formulations having recited pharmacokinetic properties, one skilled in the art would not have anticipated success in achieving the presently claimed system, as "knowledge of the goal does not render its achievement obvious." *Abbott Labs. v. Sandoz, Inc.*, 89 USPQ at 1172 (affirming the district court's determination that Abbott is likely to prevail

in its claim that the patent is valid, and upholding the grant of a preliminary injunction). We respectfully submit that the rejection has done no more than launch "metaphorical darts" based on the present disclosure where numerous formulation/delivery options would have been known, and for this reason alone the rejection must be withdrawn.

With regard to the secondary document cited by the Examiner, Green, it is respectfully submitted that Green bears no relevance to the amended claims which recite "[a] system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase." As noted previously on the record, Green discloses that "*particular sugars* may advantageously be used to prepare novel aerosol formulations. (Green, page 1, line 31-32) (emphasis added). Green discloses the use of sugars such as "sucrose, lactose and dextrose" in formulating for delivery of a particular medicament. (Abstract, and page 4, lines 22-24). Green's use of simple, single unit sugars of a molecular weight of about 180-342 in formulating, for aerosol delivery, a particular medicament provides not the slightest suggestion, motivation or expectation of success in the use of a glycosaminoglycan in the claimed system for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase, and where the glycosaminoglycan has a molecular weight of between about 50,000 and 1.5×10^6. It is submitted that Green must be removed as a cited document from the rejection. Accordingly, for this reason also, the rejection must fall.

It is submitted that based on the foregoing, the rejection has been overcome.

In addition, it is submitted that the Examiners' repeated assertions that the disclosures of Horton and McKee which were referred to by Applicants would not be considered because "the rejection ... was not made by applying Horton and McKee references", constitute legal error. Indeed, the Examiner's repeated attempts to run away from Horton and McKee are telling and evidence a recognition that they severely undermine the rejection. For example, the Manual of Patent Examining Procedure ("MPEP") instructs that the Examiner "should consider all rebuttal arguments and evidence presented by applicants" when reevaluating any obviousness determination. MPEP § 2144.08 (II)(B). As the MPEP also indicates, "[rebuttal evidence] may ... include evidence of the state of the art, the level of skill in the art, and the beliefs of those skilled in the art.... Consideration of rebuttal evidence and arguments requires Office personnel to weigh the proffered evidence and arguments." (Id.) "The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness." MPEP § 2145 (X)(D)(3).

There is no requirement in law, contrary to the Examiner's presumption, that the only documents that may be considered by the Examiner must be cited by the Examiner in an art rejection. "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art...". MPEP § 2123 (I). In fact, "in certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date." MPEP § 2124. For instance, in determining the level of ordinary skill in the art, "[r]eferences which do not qualify as prior art because they postdate the claimed invention may be relied upon to show the level of ordinary skill in the art at or around the time the invention was made." *Ex parte*

Erlich, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992); MPEP § 2141.03. Because a document used to show factual evidence need not be prior art, it stands to reason that it also need not be a document cited by the Examiner in making an art rejection.

The Examiner has turned a blind eye to evidence in the art that published subsequent to the filing of Cantor. The Horton and McKee evidence must be considered, however, rather than being dismissed as "irrelevant". As instructed by the MPEP, "the content of the prior art is determined at the time the invention was made to avoid hindsight." MPEP § 2141.01 (III) Heading. It is submitted that Horton and McKee evidence the fact that after the filing date of Cantor, the art contains reports of a pro-inflammatory response associated with low molecular weight hyaluronic acid before or at about the time the claimed invention was made. The Examiner must consider this evidence as part of the art as a whole. As note above, the Examiner simply cannot run away from Horton and McKee.

In addition, it is submitted that the Examiner has taken an unduly narrow view of Horton and McKee in dismissing the documents as "irrelevant". We refer the Examiner to the summaries of and arguments concerning Horton and Mckee in the Response dated November 21, 2007. We also direct the Examiner's attention to disclosure in the Specification regarding the Background of the Invention on page 2 which lists numerous "[i]nflammatory conditions of the respiratory tract [including] asthma, chronic obstructive pulmonary disease", etc. (Page 2, lines 1-9.) The Specification also discloses that in such inflammatory disorders, a lung tissue injury is related to the "influx of inflammatory cells, such as neutrophils, macrophages, and eosinophols." (Page 2, lines 10-13.) These "[i]nflammatory cells release noxious

enzymes [such as] [e]lastase enzymes [which] degrade elastic fibers (elastin) in the lung." (Page 2, lines 13-15.) "The damage caused by elastase enzymes may cause [further changes] which may trigger a cascade that attracts additional inflammatory cells to the lung .... and a 'vicious cycle' of lung tissue damage ensues." (Page 2, lines 16-19.) Thus, one skilled in the art hypothetically looking to achieve a system "for pulmonary delivery to a mammal of an inhalable aerosol mist of a glycosaminoglycan in an amount effective to coat elastic fibers of the lung to protect the fibers from injury by an elastase" would seek to avoid inflammatory effects.

Returning to Horton and McKee, the Examiner has asserted that "it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250kDa...". Initially, we submit that the Examiner has mistakenly characterized the claims which recite "[a] system", as a "composition". Next, it is submitted that whereas the Examiner has acknowledged that Cantor does not disclose a molecular weight of hyaluronic acid, Horton and McKee evidence that one skilled in the art would not be motivated to look to the lower end of the range of molecular weights of hyaluronic acid in view of the disclosed pro-inflammatory effect. As hyaluronic acid is known to be available in molecular weights spanning the broad range of 50,000-13,000,000, disclosures such as Horton and McKee that lead one to avoid the lower end of the range are indeed relevant to the claimed system comprising a mixture comprising a glycosaminoglycan having a molecular weight of between about 50,000 and 1.5×10^6. As recognized by the MPEP, "proceeding contrary to accepted wisdom in the art is evidence of nonobviousness." MPEP § 2145 (X)(D)(3); *In re Hedges*, 228 USPQ 685 (Fed. Cir. 1986) (Applicant's claimed process for sulfonating a

compound at a given temperature was contrary to accepted wisdom because the prior art suggested using lower temperatures for optimum results as evidenced by charring, decomposition, or reduced yields at higher temperatures.) In the present case, use of molecular weights of glycosaminoglycans at the lower range of molecular weights in a system for pulmonary delivery to a mammal would be contrary to the accepted wisdom of one skilled in the art of avoiding art-reported incidents of inflammation. As such, one skilled in the art would not have been motivated to choose molecular weights at the lower range. Furthermore, Horton and McKee would tend to lead one skilled in the art away from the presently claimed system.

With regard to experimental results in relation to the claimed invention, the Specification discloses that "[p]ossible inflammatory changes resulting from the aerosolized HA" were not seen. (Page 41, line 13-16). As stated, "[a]nimals receiving HA showed no difference from controls exposed to aerosolized water for a similar period of time." (Page 41, lines 15-16.) The Specification further discloses that "aerosolization of HA does not cause pulmonary inflammation." (Page 43, line 23-24.) In addition, it is noted that not only the effects of pancreatic elastase were tested, but also neutrophil elastase, which is "involved in the pathogenesis of human emphysema." (Page 43, lines 11-16.) "The fact that HA is effective against neutrophil elastase increases the possibility that it may be useful in limiting alveolar damage occurring in emphysema. Furthermore, the ubiquity of neutrophil elastase in various lung inflammatory reactions suggests ... that HA may be effective against other forms of pulmonary injury as well." (Page 43, lines 17-20.) Thus, one skilled in the art would understand that injury due to inflammation, and injury due to an elastase prevalent in

various lung inflammatory reactions, is not seen in connection with the claimed system, whereas this would not have been expected or predicted in view of Horton and McKee.

For each of the foregoing reasons, the rejection has been rendered moot as to all rejected claims. Reconsideration and withdrawal of the rejection is requested.

In addition with regard to the evidence of pro-inflammatory effect provided by way of Horton and McKee, the Examiner has not addressed claims 46 and 47 which recite molecular weight ranges under 250 kDa, the value cited by the Examiner. It is submitted that claims 46 and 47 are patentable for reasons separate from and in addition to the reasons for which the remaining claims are patentable.

In this regard we also reiterate from arguments previously submitted on the record that the Specification discloses the results of a protection assay testing the ability of gylcosaminoglycans to protect elastic fibers from digestion by an elastase in cell culture. (Example 15, pages 48-54.) Among other glycosaminoglycans tested, hyaluronic acid of defined molecular weights of about 227 KDa, 587 KDa, and 890 KDa was tested. (Page 49, line 24-27; page 51, line 15 – page 52, line 14; page 53, lines 1-5 and lines 20-22; Figure 13b.) It was found that "[t]he HA molecules seem to have a protective effect that varies inversely with size." The Specification discloses that the 227 KDa hyaluronic acid showed the best protective effect of the hyaluronic acid tested.

Applicants have identified the preferred molecular weight hyaluronic acid of those tested as 227 KDa, whereas one skilled in the art would not have been motivated to choose such a low molecular weight glycosaminoglycan as recited in claims 46 and 47. Moreover, the Horton and McKee evidence of pro-inflammatory

response would have dissuaded one skilled in the art from such lower molecular weights.

Reconsideration of the rejection with respect to the arguments in favor of the separate patentability of claims 46 and 47 is requested.

In view of all of the foregoing, entry of the amendments and withdrawal of all outstanding rejections are respectfully requested. It is submitted that the application is in condition for allowance. Issuance of a Notice of Allowance is respectfully requested.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 10, 2009.

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Respectfully submitted,

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